Complications associated with the treatment for spinal ependymomas

Daniel T. Nagasawa, B.A., Zachary A. Smith, M.D., Nicole Cremer, Christina Fong, Daniel C. Lu, M.D., Ph.D., and Isaac Yang, M.D.

1Department of Neurological Surgery, University of California Los Angeles; and 2Los Angeles Spine Clinic, Good Samaritan Hospital, Los Angeles, California

Spinal cord ependymomas are rare neoplasms, comprising approximately 5% of all CNS tumors and 15% of all spinal cord tumors. Although surgery was once reserved for diagnosis alone, the evolution of surgical practices has elevated resection to the treatment of choice for these lesions. Spinal cord ependymomas are predominantly slow-growing, benign tumors that tend to compress adjacent structures rather than infiltrate cord parenchyma, resulting in associated symptoms. In order of decreasing frequency, presentation may include neck or back pain, sensory deficits, motor weakness, and bowel and bladder dysfunction.

The WHO classified ependymomas into 4 distinct subtypes: subependymomas, myxopapillary ependymomas, classic ependymomas, and anaplastic ependymomas. Spinal ependymomas may affect any age group, but they are typically found in adults and comprise the myxopapillary or classic subtypes. Myxopapillary ependymomas are generally encapsulated and reside primarily in the conus medullaris, but may extend to the cauda equina. Classic ependymomas generally form in the cervical spine, but occasionally develop in the thoracic region (Fig. 1).

While the prognosis for spinal ependymomas is generally very good, there are a number of potential complications associated with their treatment that necessitate a greater awareness. As such, identification and prevention of these key issues may allow for improved outcomes in this patient population.

Resections and Progression-Free Survival

Although surgery was once reserved for diagnosis alone, the evolution of surgical practices has elevated resection to the treatment of choice for these lesions. Advances in neuroimaging, intraoperative ultrasonography, electrophysiological cord monitoring, and microsurgical techniques have afforded gross-total resections and thus decreased the risk of recurrence. The presence of neurological deficits and deterioration are not uncommonly associated with spinal cord ependymoma surgery, including sensory loss, dorsal column dysfunction, dysesthetic syndrome, and bowel and bladder dysfunction, particularly in the immediate postoperative period. Surgical treatment may also lead to wound complications and CSF leaks, with increased risk when radiotherapy has been involved. Radiation therapy may also predispose patients to radiation myelopathy and ultimately result in neurological damage. Additionally, resections of spinal ependymomas have been associated with postoperative spinal instability and deformities, particularly in the pediatric population. Despite the advances in microsurgical techniques and intraoperative cord monitoring modalities, there remain a number of serious complications related to the treatment of spinal ependymoma tumors. Identification and acknowledgment of these potential problems may assist in their prevention, early detection, and increased quality of life for patients afflicted with this disease.

Key Words: complication, ependymoma, spine, surgery, treatment
The presence of neurological deficits and deterioration are not uncommon complications associated with spinal cord ependymoma surgery. Such complications may be particularly incapacitating and slow the patient’s progress toward rehabilitation. As preoperative functional status has been assessed as a strong predictor of postoperative functional outcome, it is commonly agreed that early diagnosis and intervention are critical to optimizing neurological status. Thus, treatment should not be postponed until symptomatic functional decline, as severe or long-standing preoperative deficits rarely improve regardless of optimal surgical outcome.

While few studies have assessed postoperative neurological function in patients with spinal cord ependymomas, the majority of patients are said to be prone to increased neurological deficits immediately following resection. Surprisingly, those with minimal preoperative impairments may develop particularly pronounced symptoms. However, patients with minor preoperative complaints have experienced a greater resolution in these deficits than those having more severe preoperative functional symptoms. Such complications are believed to result from a disruption of adjacent microvasculature and edema caused by surgical manipulation of surrounding tissue. Additionally, tumors originating in the thoracic spine also incur a worse functional prognosis, perhaps due to poor microcirculation and a relatively narrow spinal canal within this region.

The McCormick classification scheme is a grading system to characterize the extent of sensorimotor deficit. In a series of 57 patients, 86% had stable or improved McCormick grades in the immediate postoperative period, whereas 7% experienced a permanent decrease in neurological function. Reports in the literature have similar findings, with 42% – 94% of patients achieving improvement of neurological deficits, while neurological decline occurred in 6% – 29%. While these deficits may not return to their preoperative status, they tend to resolve within 3 months. However, improvement in neurological complications may be appreciable as early as 4 weeks postoperatively and take up to a year to resolve, if ever.
Sakai and colleagues\textsuperscript{108} reported outcomes for 20 patients with myxopapillary spinal ependymomas. Postoperative neurological deterioration was detected in 5 (71\%) of 7 patients with unencapsulated ependymomas, while no such complications were observed in 13 patients with encapsulated tumors. Two of those with neurological deficits underwent piecemeal gross-total resection, while the other 3 underwent subtotal resections. As such, it has been suggested that tumor encapsulation may serve as a potential indicator for extent of resection and subsequent postoperative neurological function.

The dictum for resection of spinal cord tumors is to preserve eloquent tissue. In cases in which the ependymoma emerges close to the dorsal surface, a midline myelotomy is advocated as a natural plane of dissection to avoid injury of axonal tracts.\textsuperscript{77} Recognition of the accurate midline prior to myelotomy is essential to minimizing neurological defects. The midline in a normal cord is identified by the dorsal median sulcus between the elevated posterior columns (Fig. 2). The entry point of the dorsal median sulcal vein into the midline raphe, as well as the midway point between the opposing root entry zones, may be useful when approximating the medullary midline.\textsuperscript{135} While some institutions also rely on identification of posterior spinal arteries in the healthy spinal cord proximally and distally to the tumor to estimate their myelotomy incision site, others use ultrasonography and dorsal cord mapping to localize surgical landmarks.\textsuperscript{70,72}

As dorsal column manipulation is an inherent component of spinal cord ependymoma resection, one of the most serious neurological complications is dorsal column dysfunction.\textsuperscript{79} The dorsal columns of the spinal cord conduct sensory information associated with proprioception, deep touch, pressure, 2-point discrimination, and vibration.\textsuperscript{82} Occasionally, resection may become complicated by cord edema, arachnoid fibrosis, or capillary neovascularization, resulting in cord rotation, asymmetrical enlargement, and obscured delineation of the medullary midline.\textsuperscript{135} This can result in an unintentional myelotomy through the dorsal column and subsequent sensory defects, including proprioception loss with secondary gait instability.\textsuperscript{28,35,52,26,79,30,114} As the thermal energy emitted

\begin{figure}
\centering
\includegraphics[width=\textwidth]{anatomy.png}
\caption{Illustrations depicting the anatomy of a normal spinal cord demonstrating the dorsal median sulcus between the elevated posterior columns (A), cord rotation and enlargement secondary to syrinx formation (B), and midline distortion secondary to an intramedullary tumor (C). Reprinted with permission from Yanni DS et al: J Neurosurg Spine 12:623–628, 2010.}
\end{figure}
from bipolar electrocautery may cause damage to adjacent spinal tracts, the utilization of sharp dissection in the plane of spinal fibers is the preferred method around these vital areas during tumor resection. Furthermore, debulking the center of the tumor early may aid in establishing the tumor/spinal cord plane prior to dorsal column retraction. Additionally, one author noted that pial retraction stitches may increase the tension on the dorsal columns, and thus should be avoided if possible to reduce the potential damage to these sensitive structures.

Halvorsen and colleagues reported that 28% of 85 patients experienced deterioration of neurological function in the period immediately following surgery, two-thirds of which were due to midline myelotomy. Within this study, 75% of morbidity comprised dorsal column dysfunction. Similarly, Kucia and colleagues presented data in 67 patients with intramedullary ependymomas who underwent resection utilizing modern surgical approaches. Although 26 of their patients developed postoperative dorsal column deficiencies, 23 of these were McCormick Grade I or II at final follow-up.

Another potential neurological complication is dysesthetic syndrome. This phenomenon is a frequent occurrence in the early postoperative period and is found to vary substantially in severity. While some patients report occasional mild sensations of numbness and “pins and needles,” others are tormented by persistent causalgia-like dysesthesias described as “itching,” “crawling,” or “burning.” It has been suggested that damage to the dorsal columns or to the dorsal root entry zones during surgical manipulation may be responsible for the appearance of this complication.

Hanbali and colleagues reported that 56% of patients who were pain free prior to surgery developed moderate postoperative pain. Of 26 total patients in their series, 61% reported minimal pain within 4 weeks of their surgery, with 84% symptomatic within 6 months. Although the symptoms of dysesthetic syndrome tend to be refractory to medical therapy, they usually self-resolve within several months. However, McCormick and colleagues reported that 2 of 23 patients remained symptomatic 1 year after surgery.

While preoperative dysesthesia has been identified as a predictive factor for postoperative dysesthetic syndrome, Peker and colleagues determined that intramedullary ependymoma length could also be used as a risk factor. As longer tumors require longer myelotomies, this increases the potential for dorsal column injury. In accordance with this theory, Epstein and colleagues attempted to conduct atraumatic myelotomies, but were unable to attain a more significantly optimal outcome.

The impairment of bowel and bladder function is another neurological complication associated with spinal cord ependymomas, particularly seen in myxopapillary tumors originating at the conus medullaris. McCormick and colleagues reported that 5 of 23 patients experienced bowel and bladder dysfunction in the preoperative period. Three of these patients had conus tumors, 2 of which progressed to permanent worsening of the patients’ dysfunction. Bagley and colleagues examined neurological function in the pediatric population, reporting that 3 children developed bowel and bladder difficulties following their first, second, or third resection.

However, literature on pediatric spinal ependymomas suggests that the young population tends to have a favorable outcome, as 75%–93% of patients develop stable or improved postoperative neurological function. Furthermore, it has been suggested that age may be a prognostic indicator, as a review of pediatric patients determined that the likelihood of postoperative neurological abnormalities increases by 9% for each increasing year in patient age. It is speculated that similar to the developing brain, the pediatric spinal cord may possess an intrinsic level of plasticity with compensatory mechanisms to accommodate a limited degree of surgical disruption to native structures.

Neurophysiological Monitoring

Given the possible complications related to the resection of spinal ependymoma tumors and their subsequent affect on postoperative function, various techniques of neurophysiological monitoring have been used to decrease surgical morbidity. Yanni and colleagues reported results from their combined approach with intraoperative functional dorsal column mapping, preoperative radiographic imaging, and intraoperative ultrasonography to identify the most appropriate location for their midline myelotomy. A miniature multielectrode spinal cord grid was used to define the amplitude gradient of conducted SSEPs following bilateral tibial nerve stimulation, thereby correlating the functional anatomy of the patient with the surgical anatomy of the dorsal column. These data were interpreted intraoperatively by the neurophysiology team to more precisely locate the optimal plane of dissection for their midline myelotomy and avoid neurological injury. In 7 of 10 patients, the midline could not be defined with certainty by anatomical means alone. However, the utilization of dorsal column mapping and other neurophysiological monitoring techniques resulted in unilateral posterior column dysfunction in only 2 patients.

Damage to the posterior columns due to either incision or retraction results in SSEP changes with decreased amplitude and/or increased latencies. In addition, MEPs and D-waves are also often advocated as useful neurophysiological monitoring techniques. Motor evoked potentials are achieved following transcranial electrical motor cortex stimulation. The single stimulus technique elicits D-waves, allowing analysis of peak-to-peak amplitude using epidural electrode recordings. The multipulse stimulation approach evokes EMG feedback from the peripheral muscles. Potential injury to fibers of the motor pathways is indicated by loss of MEPs and/or decreased D-wave amplitude. In such instances, irrigation with warm saline and elevation of mean arterial blood pressure to optimize spinal cord perfusion may allow potentials to recover. Thus, intraoperative neurophysiological monitoring can potentially warn the surgeon of impending physiological deterioration of spinal cord integrity prior to irreversible neurological injury.

However, some reports have failed to identify a statistically significant increase in prognosis with the utilization of neurophysiological monitoring techniques. In
their small study of 17 patients, Alkhani and colleagues\(^6\) reported that patients did well regardless of monitoring status. As SSEP monitoring alone may result in false-negative responses and be insufficient for accurately predicting motor outcome, multimodal intraoperative monitoring is often recommended.\(^6,11,65,75,132\) Aside from those already described, other methods include free running EMG, evoked EMG, compound muscle action potentials, and rectal/urinary sphincter EMG.\(^65,68,96,119\) Again, while none of these modalities can independently provide a holistic evaluation of spinal cord and root integrity, their use in combination can allow surgeons to proceed with enhanced precision and confidence that the risks of neurological damage have been minimized.\(^65\)

While the advantages of neurophysiological monitoring have been demonstrated in a number of studies regarding thoracolumbar spinal lesions, data regarding its use for operations involving the cervical spine are limited.\(^3,31,50,65,69\) Given the low incidence of new postoperative neurological deficits for surgeries in this region, SSEP inaccuracy and suboptimal sensitivity make this a poor choice for single-modality monitoring.\(^55,25\) In fact, isolated injury to the motor tracks with sparing of the sensory pathways may allow false-negative responses and result in postoperative deficits.\(^55,132\) Although MEPs can offer superior sensitivity and specificity for evaluating motor integrity, MEP monitoring is more technically challenging than SSEP monitoring. Additionally, EMG monitoring is also considered a very sensitive technique, but it lacks specificity.\(^50,65,69\) Given the potentially devastating impact of a neurological injury at the cervical level, Keller and colleagues\(^65\) recommended intraoperative monitoring in all operations with neurological risk despite the low incidence of neurological complications. As no single monitoring modality appears optimal alone, multimodal monitoring may be the best approach. This is particularly applicable for patients with preexisting cord deterioration, as this population has demonstrated a higher risk for intraoperative cord compromise.\(^65,73,125\) As the utilization of SSEPs in conjunction with either continuous EMG activity or MEPs can detect most intraoperative cord injuries, their implementation in concert provide independent and complementary feedback to enhance surgical precision, decision-making strategies, and patient safety.

However, a limitation of neurophysiological monitoring is the inherent inability to accurately record data from the spinal cord with severe preoperative dysfunction seen in patients with myelopathy, trauma, or intramedullary tumors. As these cases are the ones in which cord monitoring may be the most useful, further refinement of spinal cord monitoring techniques will be necessary to optimize surgical management in this population.\(^65\)

**Spinal Instability and Deformities**

Another complication associated with surgery for spinal cord ependymomas is spinal instability and de-
Postoperative kyphosis is of particular concern for tumors of the cervical and lumbar spine, as these regions lack a rib cage that can function as an internal brace providing biomechanical support for the thoracic levels. Furthermore, the pediatric population is at an increased risk for progressive spinal deformities due to the horizontal orientation of their facet joints, a decreased elastic modulus (increased ligament laxity seen in children), and dynamic growth of the osseous spine. Spinal cord tumor resection has resulted in spinal deformities in 16%–100% of pediatric patients. Spinal cord tumor resection has resulted in spinal deformities in 16%–100% of pediatric patients. The native curvature becomes straight and then progressively kyphotic as the anterior column becomes compressed and the posterior tension band fails to maintain the integrity necessary to preserve normal alignment.

Risk factors for developing a postoperative spinal deformity include prior resection, age younger than 13 years, surgical involvement of the thoracolumbar junction, syrinx formation, exposure to spinal radiotherapy, and preoperative scoliosis. Being cognizant of these risk factors may allow surgeons to prevent such complications, detect the early onset of spinal instability, and mitigate neurological deterioration.

Historically, surgical procedures for spinal tumors included laminectomies to access the spinal cord, resulting in removal of the posterior osseous components. This technique allows for a wide exposure and can be easily extended. However, laminectomies can ventrally shift the weight-bearing axis of the normally lordotic cervical spine due to loss of the posterior ligamentous and osseous components. Consequently, the native curvature becomes straight and then progressively kyphotic as the anterior column becomes compressed and the posterior tension band fails to maintain the integrity necessary to preserve normal alignment.

In a cadaveric model, Nowinski and colleagues reported significantly increased spinal instability following cervical laminectomy with more than 25% facetectomy as compared with patients undergoing laminoplasty procedures. Other studies have suggested that resection of more than 50% of the facet capsule alone may result in stability complications. As such, to prevent spinal instability and deformity, surgeons should minimize resection of these crucial structures when possible.

To preserve these elements and optimize spinal stability, many surgeons began incorporating laminoplasty into their resections, which replaces bone and results in partial restoration of the posterior tension band. However, studies on the efficacy of this technique to reduce spinal instability have produced inconclusive results. McGirt and colleagues reported a study investigating the pediatric population and found that spinal deformities requiring fusion developed in 30% of patients who underwent laminectomy, compared with 5% of patients following the utilizing of laminoplasty. Kucia and colleagues reported 2 (7%) of 27 adults who developed spinal instability after resection of their intramedullary tumors with laminectomies, whereas none of their 40 adult patients who underwent laminoplasty developed such problems. However, in support of a 2003 meta-analysis in which the authors found no such discrepancy in postoperative spinal deformities between laminoplasty and laminectomy treatment groups, in a series of 238 patients McGirt et al. reported that the risk of spinal deformity was not significantly different between the two procedures regardless of tumor location (intramedullary vs extramedullary, cervical vs thoracic vs thoracolumbar), age, or preoperative misalignment (sagittal or coronal). However, their study was not sufficiently powered to address concerns of spinal instability beyond 2 years postoperatively. As such, future prospective studies with longer follow-up will be necessary to evaluate the long-term benefits of laminoplasty on spinal deformities.

For spinal ependymomas located in the ventral and lateral locations, a variant of the traditional surgical approach may be necessary. Lu and Lawton reported a series of operations for intramedullary spinal cord cavernous malformations utilizing unilateral radical facetectomies and partial medial pedicle resections coupled with resection of the dentate ligaments to facilitate safe manipulation of the spinal cord and allow access to the ventral surface. They also noted that while radical facetectomy...
Complications and treatment for spinal ependymomas

may theoretically result in spinal instability, no such occurrence developed when this technique was executed unilaterally for a single level.

While controversial, the practice of prophylactic spinal fusion during the initial surgery may prevent progressive spinal deformities. In one series of 33 pediatric patients with intramedullary spinal cord tumors, Simon and colleagues reported that 13 (62%) of 21 patients who received laminectomy or laminoplasty developed significant spinal deformities. Conversely, only 3 (25%) of 12 children who received spinal fusion at the time of initial surgery demonstrated similar instability. However, in a series of 22 adult patients, Lu and colleagues did not observe any cases of spinal deformities following laminectomy, even when crossing the cervicothoracic or thoracolumbar junctions. As such, while spinal fusion is not necessary in every case, patients with significant risk factors for postoperative spinal instability may be good candidates for prophylactic spinal fusion.

From our experience, the decision to implement instrumentation in adults may rely on several factors, including preoperative spinal alignment, location of the tumor, and the levels of involvement. For tumors of the cervical spine, instrumented fusion is often performed for lesions spanning 3 or more spinal levels or in patients with preoperative kyphosis. In the lumbar spine, instrumented fusion is often not necessary if the laminectomy is performed without violation of the facet joints. However, in cases with significant preoperative spondylolisthesis and instability, instrumentation may be necessary. Furthermore, for large tumors of the thoracic spine, a posterolateral approach (transpedicular, costotransversectomy, or lateral extracavitary) may be optimal and necessitate subsequent fusion.

Adjuvant Therapy

Radiotherapy

While advances in the modern surgical approach to spinal ependymoma treatment have resulted in reduced morbidity and mortality, the role of postoperative radiotherapy continues to be controversial.

Although there remains a great deal of debate regarding the utilization of postoperative radiation following gross-total resection of a spinal ependymoma, most current studies do not promote its application in this patient population as a necessary treatment. However, Akyurek and colleagues reported that 13 (62%) of 21 patients who received laminectomy or laminoplasty developed significant spinal deformities. Conversely, only 3 (25%) of 12 children who received spinal fusion at the time of initial surgery demonstrated similar instability. However, in a series of 22 adult patients, Lu and colleagues did not observe any cases of spinal deformities following laminectomy, even when crossing the cervicothoracic or thoracolumbar junctions. As such, while spinal fusion is not necessary in every case, patients with significant risk factors for postoperative spinal instability may be good candidates for prophylactic spinal fusion.

From our experience, the decision to implement instrumentation in adults may rely on several factors, including preoperative spinal alignment, location of the tumor, and the levels of involvement. For tumors of the cervical spine, instrumented fusion is often performed for lesions spanning 3 or more spinal levels or in patients with preoperative kyphosis. In the lumbar spine, instrumented fusion is often not necessary if the laminectomy is performed without violation of the facet joints. However, in cases with significant preoperative spondylolisthesis and instability, instrumentation may be necessary. Furthermore, for large tumors of the thoracic spine, a posterolateral approach (transpedicular, costotransversectomy, or lateral extracavitary) may be optimal and necessitate subsequent fusion.

Adjuvant Therapy

Radiotherapy

While advances in the modern surgical approach to spinal ependymoma treatment have resulted in reduced morbidity and mortality, the role of postoperative radiotherapy continues to be controversial.17,133

Although there remains a great deal of debate regarding the utilization of postoperative radiation following gross-total resection of a spinal ependymoma, most current studies do not promote its application in this patient population as a necessary treatment. However, Akyurek and colleagues reported that in 35 cases of myxopapillary ependymomas, postoperative radiotherapy was able to decrease the rate of tumor progression, regardless of the extent of resection. In addition, Chao and colleagues demonstrated that at the time of initial recurrence, radiation may be able to prolong the interval until subsequent recurrences. Given the rate of recurrence for spinal ependymomas treated with surgery alone and the success of radiation as a potential salvage therapy, Al-Halabi and colleagues recommended that postoperative serial imaging be mandatory.

Conversely, radiotherapy following incomplete resection is generally recommended by most investigators.46,101,112,131,139 Gavin Quigley and colleagues examined neurological outcomes and found that 82% of their patients remained at baseline or achieved functional improvement with adjuvant radiotherapy following an incomplete resection, compared with 78% of patients with similar results who underwent complete resections of their tumors only. Several other studies have demonstrated improved survival, as well as decreased and delayed recurrence with the utilization of postoperative radiotherapy following incomplete resections.2,45,67,114,117,118,122,126,128,131,139 In addition, patients with anaplastic ependymomas or severe metastatic disease may also be good candidates for adjuvant radiotherapy.10,42,54

However, the benefits of radiation therapy must be taken into consideration with a number of potential complications. Radiotherapy may result in reactive gliosis and fibrosis, hardening of the ependymoma, and disruption of the natural dissection planes. As radiation predisposes the ependymoma to increased adherence to the spinal cord, reoperation for recurrence may be more difficult with increased morbidity.4,130,133 Radiotherapy may also destroy microvasculature within the spinal cord, increasing the susceptibility of this already sensitive and diseased structure to further surgical perturbation.133

Radiotherapy can predispose patients to radiation myelopathy and ultimately result in severe neurological damage. This potential complication has been the limiting factor for the use of postoperative radiation at many surgical centers.94,130,133 Pathological features of radiation myelopathy include asymmetrical demyelination of the lateral columns, coagulative necrosis, decreased glial response, and arteriolar wall proliferation. In rare cases, myelopathy can progress to lower motor neuron syndrome, characterized by irreversible muscle atrophy, bilateral weakness, and decreased reflexes.36

Some studies have suggested that total local radiation doses greater than 50 Gy may produce a more significant response.44,94 In their retrospective study of 85 patients with myxopapillary ependymomas, Pica and colleagues compared outcomes for patients undergoing surgery plus postoperative radiotherapy versus surgery alone. They concluded that the 5-year PFS was 82% for patients who underwent surgery plus postoperative high-dose radiotherapy, compared with 50% for surgery alone. Furthermore, there was no difference in 5-year PFS between those receiving surgery alone or surgery plus low-dose radiotherapy. In accordance with a Mayo series,101,112 they observed that high-dose radiotherapy (>50.4 Gy) may possess greater benefits than lower doses. While these higher doses may increase the patient’s risk for neurological impairments, it has been estimated that a patient receiving 55 Gy of radiation has a less than 2% risk of significant spinal cord injury.45,113

Since recurrence is predominantly a local phenomenon, prophylactic radiation exposure of the entire craniospinal axis may place the patient at an unnecessary risk for complications.43,131 Furthermore, current recommendations indicate that radiotherapy targeting the complete spinal or craniospinal regions should generally be reserved for those with metastatic disease.46

The use of radiation therapy is a controversial, albeit promising, postoperative adjuvant therapy for spinal ependymomas, which will necessitate further studies to evalu-
Lin et al.76 presented a patient with a recurrent anaplastic ependymoma. The use of chemotherapeutic agents may occur during more traditional approaches by avoiding issues of beam matching, junctions, and beam isodose.49,50 Other findings have been more encouraging. Chamberlain8 reported chemotherapy results of 10 patients with recurrent spinal ependymomas who had previously undergone surgery and radiation. Two patients demonstrated partial responses following treatment with chronic oral etoposide, while another 5 patients maintained stable disease. Fakhrai et al.51 reported clinical improvement and mild tumor regression in a patient with a platelet-derived growth factor receptor-positive spinal ependymoma treated with imatinib. Iunes and colleagues52 discussed a patient receiving postoperative carboplatin and radiotherapy for their intradural extramedullary tumor with multifocal presentation; the patient survived 2 years. Dorr et al.53 described a partial response to recombinant human interferon-α for 15 months in a patient with a spinal cord ependymoma, while Tan and colleagues54 reported a 2.75-month clinical and radiological response following treatment with aziridinylbenzoquinone (AZQ). Although the heterogeneity of chemotherapies used in these studies precludes any definitive conclusion regarding their overall efficacy, adjuvant chemotherapy warrants further inspection as a promising management strategy of recurrent spinal ependymoma tumors.52

**Leptomeningeal Dissemination**

Data regarding the appropriate management for leptomeningeal dissemination associated with spinal ependymoma tumors are also severely limited. Parker and colleagues47 reported a patient with a lumbar myxopapillary ependymoma and leptomeningeal metastasis treated with HT (TomoTherapy, Inc.). While CSI is often recommended for CNS malignancies with a proclivity for leptomeningeal spread,55,56 the authors theorized that their HT technique may prove more effective due to the larger dose per fraction and higher total dose delivered to the boost sites compared with conventional CSI methods. Furthermore, HT is stated to decrease the complexity of treatment planning by avoiding issues of beam matching, junctions, and beam gaps that may occur during more traditional approaches. Lin et al.57 presented a patient with a recurrent anaplastic ependymoma and leptomeningeal seeding managed with salvage therapy consisting of CSI with focal boost and oral chemotherapy with CCNU (1-(2-chloro-ethyl)-3-cyclohexyl-1-nitrosourea). This treatment resulted in relief of symptoms, improved quality of life, and a 34-month survival.

**Cerebrospinal Fluid Leaks and Wound Infection**

Any procedures involving intradural dissections have a heightened potential for postoperative CSF leaks.57 Patients who have undergone radiotherapy or had previous operations are at an increased risk for this complication due to poor tissue integrity.25,114 Hanbali et al.54 reported 2 of 26 patients requiring lumbar drainage for CSF leaks, both of whom had undergone previous surgeries. Kucia and colleagues59 noted 13% of 67 patients with either CSF leaks or pseudomeningoceles who underwent lumbar drainage, wound revision, and/or lumboperitoneal shunting. Gavin Quigley and colleagues60 reported 23% of 26 cases of postoperative CSF leaks, 2 of which led to culture-positive meningitis. While meticulous primary closure of the dura is the best preventative measure, fibrin glue, laminoplasty, and lumbar drain placement may be used as prophylactic tactics.57,109 In their study, Manzano et al.56 used an expansile duraplasty and a lumbar drain to widen the subarachnoid space, divert CSF, and protect against CSF leaks. Furthermore, dead space may be reduced through the utilization of laminoplasty and multilayered closures to inhibit seepage through the skin. McGirt and colleagues61 identified a trend associated with laminoplasty and decreased CSF leaks compared with resections involving laminectomies. They hypothesized that reclosure of the paraspinal muscles to the spine processes in conjunction with the replacement of laminae may aid in CSF containment. While a lumbar drain, bedrest, oversewing the incision, and tissue adhesives may be sufficient to allow for proper healing of the skin and subcutaneous tissues, a wound revision with primary closure of the dural defect may be ultimately necessary.57

Similar to CSF leaks, wound infections are also more prominent in patients with a history of prior surgeries or radiotherapy.114 While this complication is a consideration of many other surgical procedures, it may be theorized that, given the sensory deficits of spinal ependymoma patients, this population may require more attentive detail in their postoperative care. Kucia and colleagues62 reported that 9% of their patients required antibiotics and/or wound debridement for wound infections. McCormick et al.63 noted that 17% of 23 patients experienced complications related to wound infections.

**Conclusions**

Despite the advances in microsurgical techniques and intraoperative cord monitoring modalities, there remain a number of serious complications related to the treatment of spinal ependymoma tumors. Identification and acknowledgment of these potential problems may assist in their prevention, early detection, and increased quality of life for patients afflicted with this disease.

**Disclosure**

Daniel Nagasawa was partially supported by an American Brain Tumor Association grant. Isaac Yang (senior author) was partially supported by a Visionary Fund Grant and a UCLA Stein Oppenheimer grant.

Author contributions to the study and manuscript preparation include the following. Conception and design: all authors. Acquisition of data: all authors. Analysis and interpretation of data:
Complications and treatment for spinal ependymomas

all authors. Drafting the article: all authors. Critically revising the article: Yang, Nagasawa, Smith, Cremer, Lu. Reviewed submitted version of manuscript: Yang, Nagasawa, Smith, Lu. Approved the final version of the manuscript on behalf of all authors: Yang. Statistical analysis: Yang, Nagasawa. Administrative/technical/material support: Yang, Nagasawa, Smith, Lu. Study supervision: Yang, Nagasawa, Smith, Cremer, Lu.

References


Neurosurg Focus / Volume 31 / October 2011

---

Manuscript submitted June 15, 2011.
Accepted July 19, 2011.

*Address correspondence to:* Isaac Yang, M.D., Department of Neurological Surgery, University of California Los Angeles, 695 Charles E. Young Drive South, Gonda 3357, Los Angeles, California 90095-1761. email: iyang@mednet.ucla.edu.